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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/625,049	07/24/2000	Reinhilde Schoonjans	DECL18.001C1	6634

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 04/16/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/625,049

Applicant(s)

SCHOONJANS ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43-66 is/are pending in the application.
- 4a) Of the above claim(s) 51-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43,44,46-49 and 61-66 is/are rejected.
- 7) ☒ Claim(s) 45 and 50 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 43-50 and 61-66 are under examination.
2. Claims 51-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in Paper No. 10.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Response to Arguments

4. The rejection of claims 43-44, 46-49, 61-62, 64-66 under 35 U.S.C. 103(a) as being unpatentable over Carter (U.S. Patent 5,648,237, issued 7/15/97) and further in view of Chester et al (TIBTECH 13:296, 1995) is maintained.

The response filed 1/28/03 has been carefully considered but is deemed not to be persuasive. The response states that Carter does not teach or suggest heterodimers wherein the CH1 domain is not linked to a hinge region (see page 3 of response). In response to this argument, Carter clearly teaches that the hinge region can be entirely omitted in favor of a single cysteine or a cysteine containing peptide (see column 8, lines 20-25). In addition, Paul et al (Fundamental Immunology, Raven Press, page 299-300, 1993) which is cited to provide the state of the art for the definition of a hinge region of an immunoglobulin which contains numerous residues in addition to cysteines. Thus, a single cysteine is not a hinge region by definition. The response

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further states that Carter does not teach or suggest heterodimers containing at least two other molecules X and Y and Chester would not provide motivation to fuse two molecules to the Fab (see page 3 of response). In response to this argument, Chester clearly teaches molecules fused to the CL and in view of Carter et al who teaches additions of additional molecules at the C-terminus or N-terminus of the Fabs (see column 12, lines 53-57) and bivalent and bispecific molecules, it would have been obvious to couple other molecules to the c-terminus of the CL and the CH1.

5. The rejection of claims 43-44, 46-49, and 61-66 under 35 U.S.C. 103(a) as being unpatentable over Carter (U.S. Patent 5,648,237, filed 5/3/95) and further in view of Tutt et al (The Journal of Immunology 147:60-69, 1991) is maintained.

The response filed 1/28/03 has been carefully considered but is deemed not to be persuasive. The response states that Figure 1 of Tutt et al teach Fabs with hinge regions chemically coupled to phenylenediamaleimide and there is nothing in Tutt et al to teach or suggest coupling antibodies without the hinge region (see page 4 of response). In response to this argument, Tutt et al teach trispecific antibodies which are used to target wherein in combination with the teachings of Carter of Fab-SH molecules and Fabs with peptide linkers which contain a cysteine residue and bispecific molecules it would be obvious to produce trispecific Fabs with crosslinking according to Tutt et al.

Conclusion

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6. No claim is allowed. Claims 45 and 50 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

A handwritten signature in black ink, consisting of several overlapping, stylized loops and a final horizontal stroke.